IN THE CLAIMS

Claims 1, 5, 6, 46 and 50 are amended herein. Claim 51 is added. The following listing of Claims replaces all previously advanced Claim listings.

1. (Currently Amended) An isolated monoclonal antibody that binds specifically to a polypeptide comprising a ubiquitination-regulating domain, or a functional fragment thereof, of a human TSG1O1 protein comprising the amino acid sequence of SEQ ID NO: 1, wherein said antibody binds specifically to said ubiquitination-regulating domain, ~~or functional fragment thereof~~; and

wherein said antibody binds specifically to an epitope in the ubiquitination-regulating domain of TSG101 protein found in amino acid residues 1-250 of SEQ NO: 1 and by so binding, said antibody modulates interaction between said human TSG101 protein ~~or functional fragment~~ thereof and MDM2 protein .

2-3. (Cancelled).

4. (Currently Amended) An isolated monoclonal antibody that binds specifically to a polypeptide comprising a ubiquitination-regulating domain, ~~or a functional fragment thereof,~~ of a human TSG1O1 protein comprising the amino acid sequence of SEQ ID NO: 1, wherein said antibody binds specifically to said ubiquitination-regulating domain, ~~or functional fragment thereof~~; and

wherein said antibody binds specifically to an epitope in the ubiquitination-regulating domain of TSG101 protein found in amino acid residues, wherein said ubiquitination-regulating domain comprises amino acid residues 50-140 of SEQ ID NO:1, and wherein said epitope is found in amino acid residues 50-140 of SEQ ID NO:1.

5. (Currently Amended) An isolated monoclonal antibody that binds specifically to a polypeptide comprising a ubiquitination-regulating domain, or a functional fragment thereof, of a human TSG1O1 protein comprising the amino acid sequence of SEQ ID NO: 1, wherein said antibody binds specifically to said ubiquitination-regulating domain, ~~or functional fragment thereof~~; and

wherein said antibody binds specifically to an epitope in the ubiquitination-regulating domain of TSG101 protein found in amino acid residues 1-140 of SEQ ID NO: 1, and wherein said epitope is found in amino acid residues 1-140 of SEQ ID NO:1.

6. (Previously Presented) The antibody of Claim 1, wherein said ubiquitination-regulating domain comprises amino acid residues 140-250 of SEQ ID NO: 1, and wherein said epitope is found in amino acid residues 140-250 of SEQ ID NO:1.

7. (Withdrawn) A method of producing an antibody that binds specifically to an ubiquitination-regulating domain, comprising raising said antibody against a polypeptide comprising said ubiquitination-regulating domain.

8. (Withdrawn) The method of Claim 7, wherein said ubiquitination-regulating

domain is a ubiquitination-regulating domain~~, or a functional fragment thereof~~, of a TSG1O1 protein.

9. (Withdrawn) The method of Claim 8, wherein said TSG 101 protein is a human TSG1O1 protein.

10. (Withdrawn) The method of Claim 9, wherein said ubiquitination-regulating domain comprises amino acid residues 50-140 of said human TSGI 01 protein.

11. (Withdrawn) The method of Claim 8, wherein said ubiquitination-regulating domain comprises amino acid residues 1-140 of said human TSG 101 protein.

12. (Withdrawn) The method of Claim 9, wherein said ubiquitination-regulating domain comprises amino acid residues 140-250 of said human TSG1OI protein.

13. (Withdrawn) A method of treating a condition in a subject, said condition resulting from a change in a level of MDM2 protein in cells of said subject, said method comprising administering to said subject a therapeutically effective amount of an agent, said agent comprising an ubiquitination-regulating domain.

14. (Withdrawn) A method of treating a condition in a subject, said condition resulting from a change in a level of a TSG 101 protein in cells of said subject, said method comprising administering to said subject a therapeutically effective amount of an agent, said agent modulating the interaction of said TSG1OI protein with MDM2.

15. (Withdrawn-Previously Amended) A method for treatment of a proliferative disease in a subject comprising:

(a) monitoring the subject for a level of p53; and

(b) treating the subject with an agent so as to maintain said level of p53 within a target range, wherein said agent comprises an ubiquitination-regulating domain.

16. (Withdrawn-Previously Presented) A method for treatment of a proliferative disease in a subject comprising:

(a) monitoring the subject for a level of TSGI 01; and

(b) treating a subject with an agent so as to maintain said level of TSGIO1 within a target range, wherein said agent modulates the interaction of said TSG1O1 with MDM2.

17-21. (Cancelled).

22. (Withdrawn) A method for treating a proliferative disease in a subject, said method comprising administering to said subject a therapeutically effective amount of an agent, said agent modulating the interaction of a TSG1O1 protein with MDM2.

23. (Withdrawn) A cell comprising a polynucleotide encoding an ubiquitination-regulating domain operationally linked to a regulatory sequence such that said cell expresses said ubiquitination-regulating domain.

24. (Withdrawn) A cell comprising (i) a polynucleotide encoding an ubiquitination-regulating domain operationally linked to a regulatory sequence; and (ii) a polynucleotide encoding MDM2 protein operationally linked to a regulatory sequence, such that said cell expresses said ubiquitination-regulating domain and said MDM2 protein.

25. (Withdrawn) A cell comprising (i) a polynucleotide encoding an ubiquitination-regulating domain operationally linked to a regulatory sequence; (ii) a polynucleotide encoding MDM2 protein operationally linked to a regulatory sequence; and (iii) a polynueleotide encoding p53 protein operationally linked to a regulatory sequence, such that said cell expresses said ubiquitination-regulating domain, said MDM2 protein, and said p53 protein.

26-30. (Cancelled).

31. (Withdrawn) A method of identifying an agent that modulates the interaction of a TSGIOI protein with MDM2, comprising screening candidate agents using a screening assay comprising a cell expressing MDM2 and a polypeptide comprising an ubiquitination-regulating domain, or a functional fragment thereof, of said TSG1O1 protein.

32. (Withdrawn-Previously Amended) A method of identifying an agent that is capable of modulating the interaction of a TSGIO1 protein with MDM2, comprising:

(a) contacting a first cell expressing MDM2 and a polypeptide comprising an ubiquitination-regulating domain, or a functional fragment thereof, of said TSG 101 protein with said agent and measuring MDM2 level in said first cell;

(b) contacting a second cell expressing MDM2 but not an ubiquitination-regulating domain, or a functional fragment thereof, of said TSGIO1 protein, with said agent and measuring MDM2 level in said second cell; and

(c) comparing MDM2 levels measured in (a) and (b),

wherein a difference in MDM2 levels compared in step (c) identified said agent as capable of modulating the interaction of the TSG 101 protein with MDM2.

33-36. (Cancelled).

37. (Withdrawn) A method of modulating a level of MDM2 in a cell, comprising contacting said cell with a polypeptide or derivative thereof that comprises a polypeptide comprising a polypeptide comprising an ubiquitination-regulating domain.

38. (Withdrawn) A method of modulating a level of p53 in a cell, comprising contacting said cell with a polypeptide or derivative thereof that comprises a polypeptide comprising an ubiquitination-regulating domain.

39. (Withdrawn) A method of modulating a level of TSG1O1 in a cell, comprising contacting said cell with an agent that is capable of modulating the interaction of a TSG 101 protein with MDM2.

40. (Withdrawn) A method of modulating a level of MDM2 in a cell, comprising contacting said cell with an agent that is capable of modulating the interaction of a TSG 101 protein with MDM2.

41. (Withdrawn) A method of modulating a level of p53 in a cell, comprising contacting said cell with an agent that is capable of modulating the interaction of a TSG1OI protein with MDM2.

42. (Withdrawn) A method for screening for a cellular protein that interacts with an ubiquitination-regulating domain, comprising identifying a cellular protein that binds said ubiquitination-regulating domain.

43. (Currently Amended) A pharmaceutical composition for treatment of diseases involving TSG 101-mediated ubiquitination, comprising:

an isolated monoclonal antibody that binds specifically to a polypeptide comprising an ubiquitination-regulating domain, ~~or a functional fragment thereof,~~ of a human TSG101 protein comprising the amino acid sequence of SEQ ID NO:1, wherein said antibody binds specifically to said ubiquintination-regulating domain, ~~or functional fragment thereof,~~

wherein said antibody binds specifically to an epitope in the ubiquitination regulating domain of TSG101 protein found in amino acid residues 1-250 of SEQ ID NO: 1, and

a pharmaceutically acceptable excipient.

44. (Withdrawn) A method for treatment of diseases involving TSG1OI-mediated ubiquitination, said method comprising:

administering to a subject suffering from a disease involving TSG1O1-mediated ubiquitination an effective amount of the pharmaceutical composition of Claim 43.

45. (Withdrawn) The method of Claim 44, wherein the diseases involving TSG 101-mediated ubiquitination comprise proliferative diseases, neurodegenerative diseases, autoimmune diseases, and developmental abnormalities.

46. (Currently Amended) An isolated monoclonal antibody that binds specifically to a ubiquitination-regulating domain of TSG101, ~~or a functional fragment thereof,~~ wherein said domain consists of amino acid residues 1-250 of SEQ ID NO: 1, and

wherein said antibody specifically binds to an epitope in the ubiquitination regulating domain of TSG101 protein found in amino acid residues 1-250 of SEQ ID NO: 1 and by so binding, said antibody modulates interaction between said human TSG101 protein or functional fragment thereof and MDM2 protein .

47. (Previously Presented) The isolated antibody of Claim 46, wherein said ubiquitination-regulating domain consists of amino acid residues 50-140 of SEQ ID NO: 1, or a functional fragment thereof, and wherein said epitope is found in amino acid residues 50-140 of SEQ ID NO:1.

48. (Previously Presented) The isolated antibody of Claim 46, wherein said ubiquitination-regulating domain consists of amino acid residues 1-140 of SEQ ID NO: 1, or a functional fragment thereof, and wherein said epitope is found in amino acid residues 1-140 of SEQ ID NO:1.

49. (Previously Presented) The isolated antibody of Claim 46, wherein said ubiquitination regulating domain consists of amino acid residues 140-250 of SEQ ID NO: 1, or a functional fragment thereof, and wherein said epitope is found in amino acid residues 140-250 of SEQ ID NO:1.

50. (Currently Amended) A pharmaceutical composition for treatment of diseases involving TSG 101-mediated ubiquitination, comprising:

an isolated monoclonal antibody that binds specifically to a ubiquitination-regulating domain of human TSG101, ~~or a functional fragment thereof,~~ wherein said antibody binds specifically to an epitope in the ubiquitination-regulating domain of TSG101 protein found in amino acids 1-250 of SEQ ID NO: 1; and, a pharmaceutically acceptable excipient, wherein said pharmaceutically acceptable excipient is acceptable for administration to a mammal.

51. (New) The pharmaceutical composition of Claim 50, wherein, when administered to a mammal in an amount effective for the purpose, said antibody modulates interaction between TSG101 protein and MDM2 protein in said mammal.